

Gene Section

Short Communication

SSX2IP (synovial sarcoma, X breakpoint 2 interacting protein)

Ghazala Khan, Barbara Guinn

University of Bedfordshire, Division of Science, Park Square, Luton, Bedfordshire, UK (GK), University of Bedfordshire, Division of Science, Park Square, Luton, Bedfordshire, UK; Cancer Sciences Unit, University of Southampton, Southampton, UK; Department of Haematological Medicine, Kings College, London, UK (BG)

Published in Atlas Database: March 2012

Online updated version : <http://AtlasGeneticsOncology.org/Genes/SSX2IPID42407ch1p22.html>
DOI: 10.4267/2042/47489

This work is licensed under a Creative Commons Attribution-Noncommercial-No Derivative Works 2.0 France Licence.
© 2012 Atlas of Genetics and Cytogenetics in Oncology and Haematology

Identity

Other names: ADIP

HGNC (Hugo): SSX2IP

Location: 1p22.3

Note

SSX2IP gene encodes the protein SSX2IP which interacts with the cancer-testis antigen SSX2. It is thought that SSX2IP regulates the function of SSX2 in the testes and malignant cells. The rodent equivalent is known as afadin DIL domain-interacting protein (ADIP) and the chicken orthologue is called clock-controlled gene (LCG) (Breslin et al., 2007).

DNA/RNA

Note

The SSX2IP gene is located on chromosome 1p22.3 (Entrez Gene).

Description

SSX2IP includes over 46 kb and consists of 14

exons however the first one is not translated (de Bruijn et al., 2002).

Transcription

The gene contains 33 introns. 18 different mRNAs are produced; 17 spliced and 1 un-spliced form (Thierry-Mieg and Thierry-Mieg, 2006).

Pseudogene

A pseudogene of this gene is found on chromosome 3 (provided by RefSeq, Oct 2009 from Entrez Gene).

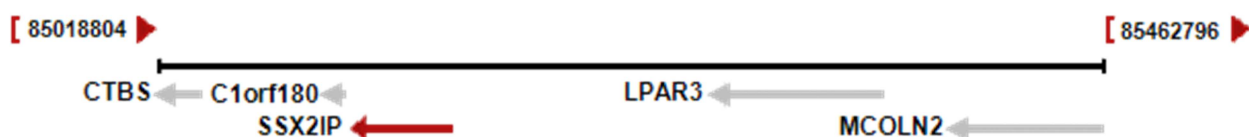
Protein

Note

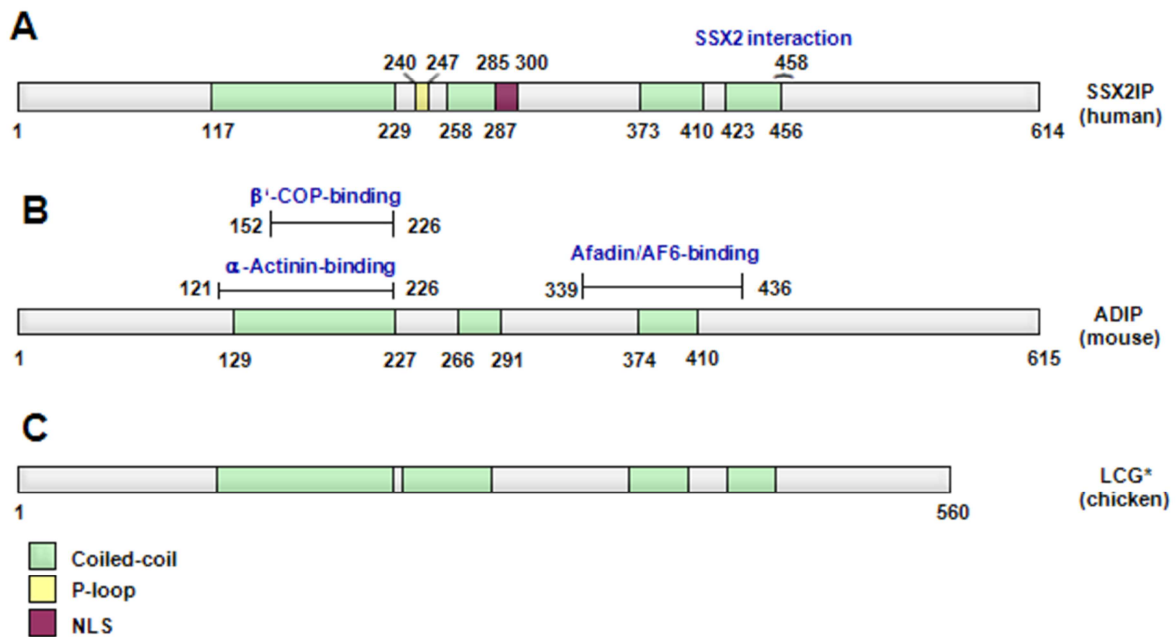
SSX2IP was discovered due to its interaction with SSX2 in a yeast two-hybrid system and believed to regulate the function of SSX2 in the testes and malignant cells (de Bruijn et al., 2002).

Description

There are 3-4 coil coiled regions in each version of SSX2IP. Only human SSX2IP has a nuclear localisation signal (NLS).



Location of SSX2IP gene on chromosome 1 and the surrounding region.



Structural representation of SSX2IP protein in human, mouse and chicken showing the binding regions (Breslin et al., 2007).

Expression

Expression observed in various normal tissues, the highest being in the brain (de Bruijn et al., 2002). It is expressed less but significantly in kidney, testes, spinal cord, liver, heart, lung, pancreas, skeletal muscle, ovary, placenta, foetal liver and foetal brain (Breslin et al., 2007).

Localisation

SSX2IP co-localises with SSX2 to the nucleus and some fragments to the cytoplasm (de Bruijn et al., 2002).

It has also been seen to localise on the surface of myeloid cell lines and primary AML (Denniss et al., 2007).

ADIP co-localises with afadin at adherens junctions and in perinuclear regions (Asada et al., 2003).

Function

It has been suggested that SSX2IP regulates the function of SSX2 (de Bruijn et al., 2002).

Rodent ADIP binds with F-actin binding proteins afadin and α -actinin and could therefore be involved in forming actin structure at cell-cell adherens junction as well as construction of actin bundle at nectin-based cell adhesion sites (Asada et al., 2003).

Through its interaction with the actin-binding protein β -spectrin, ADIP may have a role in actin-dependent organization of the Golgi complex. ADIP binds β' -cop, which is a subunit of the coatamer complex, proposing a role in vesicle trafficking (Asada et al., 2004).

Implicated in

Acute myeloid leukaemia

Note

SSX2IP expression has been seen to be elevated in 33% of acute myeloid leukaemia patient samples at presentation (Guinn et al., 2005).

Peak expression on the surface of myeloid leukaemia cells is during mitosis (Denniss et al., 2007). Patients with the t(15;17) translocation have increased levels of SSX2IP whereas expression is decreased in patients with the t(8;21) translocation (Guinn et al., 2008).

Prognosis

Patients with no chromosomal abnormalities showed improved survival rates with elevated expression of SSX2IP.

High level of SSX2IP expression is associated with other positive prognostic markers such as days in remission and age at diagnosis (Guinn et al., 2009).

Cytogenetics

The t(15;17) translocation leads to PML-RAR α product.

Overexpression of PML during the cell cycle leads to G1 arrest in normal fibroblasts which cannot occur once PML attaches to RAR α .

Genes regulating cyclin dependent kinase activity are upregulated in correlation with overexpression of SSX2IP.

The t(8;21) translocation generates the AML1-ETO fusion product.

Cells with this gene product develop aneuploidy due to decreased regulation at the spindle checkpoint.

Low levels of SSX2IP relate to reduced expression of CDC20, a substrate-targeting subunit of the anaphase-promoting complex (Guinn et al., 2008).

References

de Bruijn DR, dos Santos NR, Kater-Baats E, Thijssen J, van den Berk L, Stap J, Balemans M, Schepens M, Merx G, van Kessel AG. The cancer-related protein SSX2 interacts with the human homologue of a Ras-like GTPase interactor, RAB3IP, and a novel nuclear protein, SSX2IP. *Genes Chromosomes Cancer*. 2002 Jul;34(3):285-98

Asada M, Irie K, Morimoto K, Yamada A, Ikeda W, Takeuchi M, Takai Y. ADIP, a novel Afadin- and alpha-actinin-binding protein localized at cell-cell adherens junctions. *J Biol Chem*. 2003 Feb 7;278(6):4103-11

Asada M, Irie K, Yamada A, Takai Y. Afadin- and alpha-actinin-binding protein ADIP directly binds beta'-COP, a subunit of the coatomer complex. *Biochem Biophys Res Commun*. 2004 Aug 20;321(2):350-4

Guinn BA, Bland EA, Lodi U, Liggins AP, Tobal K, Petters S, Wells JW, Banham AH, Mufti GJ. Humoral detection of leukaemia-associated antigens in presentation acute myeloid leukaemia. *Biochem Biophys Res Commun*. 2005 Oct 7;335(4):1293-304

Thierry-Mieg D, Thierry-Mieg J. AceView: a comprehensive cDNA-supported gene and transcripts annotation. *Genome Biol*. 2006;7 Suppl 1:S12.1-14

Breslin A, Denniss FA, Guinn BA. SSX2IP: an emerging role in cancer. *Biochem Biophys Res Commun*. 2007 Nov 23;363(3):462-5

Denniss FA, Breslin A, Ingram W, Hardwick NR, Mufti GJ, Guinn BA. The leukaemia-associated antigen, SSX2IP, is expressed during mitosis on the surface of myeloid leukaemia cells. *Br J Haematol*. 2007 Sep;138(5):668-9

Guinn BA, Bullinger L, Thomas NS, Mills KI, Greiner J. SSX2IP expression in acute myeloid leukaemia: an association with mitotic spindle failure in t(8;21), and cell cycle in t(15;17) patients. *Br J Haematol*. 2008 Jan;140(2):250-1

Guinn B, Greiner J, Schmitt M, Mills KI. Elevated expression of the leukemia-associated antigen SSX2IP predicts survival in acute myeloid leukemia patients who lack detectable cytogenetic rearrangements. *Blood*. 2009 Jan 29;113(5):1203-4

This article should be referenced as such:

Khan G, Guinn B. SSX2IP (synovial sarcoma, X breakpoint 2 interacting protein). *Atlas Genet Cytogenet Oncol Haematol*. 2012; 16(8):552-554.
